STATEMENT OF DR. FRANK I. MARCUS IN RESPONSE TO WARNING LETTER ISSUED TO THE UNIVERSITY OF ARIZONA, DATED APRIL 27, 2001

This statement is a response to the information contained in the Warning Letter issued by the Food and Drug Administration to Dr. Peter Likins, President, University of Arizona, dated April 27, 2001. The letter grew out of an inspection carried out at the University of Arizona from September 18-22 and October 3-6, 2000, which related to a study that I had performed in 1997 for Bard Electrophysiology, Inc., Boston, MA.

I have written this response because the letter accuses me of poor record keeping, of mismanagement and a refusal to provide records to the FDA inspectors. ***I am responding as an individual and not for the University of Arizona.***

First, I would like to provide information concerning my background. I am a Professor Emeritus at the University of Arizona and has been a member in good standing of the University faculty since January 1969. I am a clinical cardiologist with special training in cardiology and electrophysiology, and I founded the Section of Cardiology and was the chief of cardiology at the University Medical Center. I have published 250 scientific articles in peer reviewed medical journals and have contributed 52 book chapters. I am on the Editorial Board of nine cardiology journals and regularly review scientific articles for about 15 journals. My appointments in scientific societies include past President of the Association of the University Cardiologists. I was a member of the Board of Trustees of the American College of Cardiology and was founder and first President of the Arizona Chapter of American College of Cardiology. I have participated in many clinical trials in which data obtained by me and my staff have been submitted to the FDA and have never had any challenge to the veracity of this data.

Until 1997, I had not conducted animal studies for submission to the FDA in support of an application to market a medical device or drug. In 1997, Bard Electrophysiology, Inc. asked me to evaluate a new electrophysiology catheter that subsequently was approved by FDA and is now being marketed under the name "Stinger Catheter". The purpose of the study was to obtain my judgment concerning the handling characteristics of this catheter when inserted and guided to the heart of an anesthetized dog. In addition, I agreed to record electrical signals from the various cardiac chambers of the dogs heart to evaluate the clarity of these signals and to compare them with similar data obtained from a catheter that was FDA approved and manufactured by another company. Radiofrequency energy was delivered to the catheter tip, and after a suitable time the animals were sacrificed and the lesions were evaluated pathologically. The study was conducted in 1997. The catheter received approval in part from the data submitted from the study in which I participated.

Prior to initiation of the study, Bard agreed in writing to serve as the quality assurance unit for this study. The audit conducted by Bard personnel on May 14, 1997, indicated that Bard personnel deemed the site to have sufficient training, resources and expertise to adequately conduct the study. The study records provided to FDA on October 6, 2000, demonstrate that every attempt was made to insure Good Laboratory Practices compliance throughout the duration of the study from April 1997 to issuance of the final report in November 1997.

In the Warning Letter, there are repeated statements that I refused to provide records to the FDA inspector. I respectfully disagree. Not all the records required to be maintained under FDA's Good Laboratory Practice regulations were available at the site. However, I provided the inspector with all of the records in my possession. I informed the inspector that I had moved my offices in October 1999 and that it had been necessary to discard numerous records in order to find sufficient room in my new facility. At no time was any record in my possession or control withheld from the inspector, nor was the inspector ever denied access to any person in the area of the facility. *All of the records which I was not able to produce were available from BARD.*

With regard to the request for records, when the FDA inspector called me from Los Angeles on September 22nd that she would be coming to Tucson on September 25th to start the inspection, she made no specific request regarding material to be reviewed. Within the first day or two after she had arrived, I contacted [redacted], in Bard's regulatory affairs at the Bard Company. [redacted] and I were not certain as to the extent and details of the information that the inspector wanted. [redacted] placed several calls to the Tucson FDA office to ascertain what records the inspector felt were missing from those that I had given to the inspector. [redacted] later informed me that he had never received any call back from the inspector. On October 5, 2000 [redacted] participated in a conference call with the inspector and me at which time it was learned from the inspector which records were missing. [redacted] provided a complete set of duplicate records on October 6, 2000. The FDA inspectors also requested records of all animal studies I had done in the previous two years. These were unrelated to the Bard GLP study and the request was not specifically related to the FDA or any FDA-regulated product. The attorney representing the University of Arizona determined that these records were confidential and not accessible to outside parties, including the FDA. *All* records related to the Bard GLP study were made available to the FDA.

The above information addresses the major accusations in the Warning Letter directed towards me. There were a number of other allegations that were answered in the response letter sent to the FDA by the University of Arizona to correct the misunderstandings or wrongful allegations directed against me. I would like to focus on one item of importance from that letter:

The Warning Letter stated that I did not demonstrate control of the study, that I did not compile the data report, and that I was not the author of the final report submitted to the FDA. The inspector at the FDA office stated that there were at least five examples of wording differences between Bard's premarket approval submission and the report signed by me. When I asked to see the differences in wording so that I could verify that there were indeed differences, the inspector refused this request and therefore, I could not comment on any alleged differences in the wording. When I again asked the inspector on October 22, 2000 to provide me with examples of the differences, it was stated that this could not be done until the inspection was completed and the report was made. It seems unlikely to me that there were such differences. Bard personnel collected the data, served as the quality assurance unit, verified it and compiled a report in collaboration with me as evidenced by my signature on the final report. The inspector was able to review drafts that were in my possession for this current inspection. Further, data collected by the University of Arizona personnel were submitted to the inspector and these notes and reports were prepared and finalized for my signature. It continues to be my belief that the

exact same document as was signed by the study personnel, [redacted] and me was included in the PMA. Therefore, I never was able to identify any possible differences.

In conclusion, I submit that there have been many unfounded and inaccurate allegations made regarding my activities and participation in the Bard Electrophysiology study.